fascia, both as to its ease in application and the resultant histological picture. The same type of cell took part in the reaction, and at the end of a year complete absorption had occurred (Fig. 7). In a clinical case, studied eight months after the introduction of the graft, the membrane was quite apparent. It was entirely surrounded by fibrous tissue. The dura about the membrane was thicker than the surrounding area, and there were no adhesions (Fig. 8).

CONCLUSIONS

1. Experimental and clinical studies indicate that the use of either a heteroplastic or autoplastic graft for the repair of dural defects is entirely unnecessary.

2. Should one feel inclined to use a dural graft, heteroplastic animal membrane is equally as efficient as autoplastic fascia.

3. Dural defects caused by surgical procedures or depressed skull fractures without injury to the underlying arachnoid spontaneously repair themselves.

4. If the arachnoid is not injured, adhesions will not form between the dura, arachnoid and brain, but will form between the overlying skull and periosteum, as well as fascia and muscle.

5. Both types of grafts are entirely absorbed within twelve months.

6. The cells that form the new dura are apparently derived from the overlying fascia and muscle and from a peripheral outgrowth of dural cells, which arise from the cut margin of the dura.*

727 West Seventh Street.

DISCUSSION

EDMUND J. MORRISSEY, M.D. (330 Medical Building, San Francisco).—The work of Doctors Glaser and Thienes is an excellent and timely piece of experimental research. Their findings agree in all important details with similar studies reported by Sayard and Harvey, and Lear and Harvey.

In my opinion, the work shows conclusively that defects in the dura will heal without the formation of adhesions in a very short period of time, provided the underlying arachnoid has not been injured. On the other hand, if the arachnoid has been injured, adhesions will form, regardless.

Too often, however, we see the mistake being made of covering these dural defects with facial transplants, or some other foreign material, which certainly is unnecessary and which, in my opinion, will do nothing more than increase the adhesions.

FREDERICK LEET REICHERT, M.D. (Stanford University Hospital, San Francisco).—This experimental study of Doctors Glaser and Thienes confirms the clinical observations of neurosurgeons that, whether a portion of dura is excised or replaced without suture, the resultant gap is readily and completely closed by tissue which resembles dura and officiates as dura. This applies only where the pia arachnoid is intact.

In the clinical application of this experimental study, one need not be apprehensive about replacing a dural defect if overlying muscle is available; but if muscle cannot be used, a fascial graft or the prepared membrane will form a new dura. Again, this applies in cases in which the pia arachnoid is intact. Where the pia arachnoid is absent from any cause, one prefers to cover this pial defect by a plastic procedure with the patient's dura, leaving a dural defect over the intact pia arachnoid.

HOWARD W. FLEMING, M.D. (384 Post Street, San Francisco).—Doctors Glaser and Thienes's clinical and experimental studies give further substantiation to the popularly accepted theories regarding the healing processes of brain and dural tissues. The facts that dural defects repair themselves spontaneously, and that adhesions do not form if the arachnoid is uninjured, are reassuring.

In the past, surgeons often went to great extremes to effect a complete closure of the dura following operation. This, in most cases, is no longer considered necessary. There are circumstances where the use of a dural graft may be advantageous.

It is advisable to debride and repair penetrating wounds of the brain. If the patient is cared for soon after injury, a careful debridement will lessen the possibility of infection and possibly reduce the morbidity. A snug graft in the dura will minimize the contusion to the brain and prevent a fungus should a marked increase of intracranial pressure develop as a late complication. A careful repair of the dura will also allow the replacement of small fragments of bone to fill the skull defect that could not otherwise be utilized.

In the treatment of post-traumatic epilepsy, excision of a cortical scar and the overlying dura is often necessary. Repair of the dural defect is not essential, but probably advisable. Occasionally, false meningoceles develop in cases where there is a loss of bone over the dural defect.

The kind of material to be used in dural grafts depends largely upon the past experiences and the preferences of the individual surgeon. Many prefer autoplastic substances, such as temporal fascia or fascia lata, on the theory that there is less foreign-body reaction than when heteroplastic substances are used. The author's conclusion in this paper would seem to negate this idea.

Probably careful handling of tissues and hemostasis are more important than the type of material used to fill a dural defect.

* We wish to extend our sincere thanks to Dr. H. M. Beerman for his aid in the experimental surgery, and to Dr. M. Bettin and Dr. E. M. Butt for their advice in the preparation of the pathological material.

TRICHINOSIS*

By JAMES B. MCNAUGHT, M.D.
San Francisco

DISCUSSION *by John J. Miller, M. D., San Francisco; R. D. Friedlander, M.D., San Francisco; E. M. Butt, M.D., Los Angeles.*

THE Mosaic code, of some three thousand years ago, forbade the use of pork: "And the swine is unclean to you. Of their flesh shall ye not eat, and their carcass shall ye not touch."[1] Some believe that it was forbidden because the hog had been worshiped by certain heathen tribes; but modern interpreters[2] of this code maintain that Moses had noticed a peculiar train of symptoms in people who had partaken of pork, and thus condemned its use as food. For thirty centuries the Jews were ridiculed for abstaining from pork. During this time no one heard of trichinosis and, as far as is known, no one, until 1835, saw trichinella. In February of that year James Paget, then a medical student at St. Bartholomew's Hospital, London, "was dissecting the muscles of a subject, when his scalpel became quickly and repeatedly blunt."[3] He saw numerous small calcareous specks in the muscles. There was no microscope available at the hospital, but Robert Brown, the botanist, had a simple one at the British Museum through which Paget saw a worm within a capsule. He made careful sketches of the parasite, and prepared a report of his discovery for the *London Medical Gazette*;

* From the Department of Pathology, Stanford University School of Medicine.

Read before the Pathology and Bacteriology Section of the California Medical Association at the sixty-sixth annual session, Del Monte, May 2–6, 1937.

but it was never printed, although the manuscript may still be seen at the College of Surgeons. A specimen from Paget's subject was submitted to Richard Owen of the College of Surgeons, who named the parasite Trichina spiralis, and published his findings. The name was later changed to Trichinella spiralis.

Dr. Henry Bowditch[4] of Boston, in 1842, reported the first case of trichinosis in America in a young man who died from a malignant growth. Joseph Leidy[5] of Philadelphia, in 1847, demonstrated the parasite in pork. It was Zenker[6] of Dresden, who, in 1860, described clinical trichinosis. He established the connection of the parasite, which he saw in the muscles of a patient, with an illness clinically regarded as typhoid fever. He ascertained that the patient had eaten of flesh from a certain pig that had caused serious illness in everyone who had eaten it, and finally pointed out the parasites in ham and sausage from the pig in question. Within five years the people of Prussia and Saxony were in a state of panic because of fear of the disease during terrible epidemics. The German Government then instituted a method of examining pork microscopically, which is still in use. It consisted in pressing bits of muscle between glass plates and examining it, under the microscope, for the parasites. The infected animals were condemned for human consumption. Stiles[7] stated that the trichina inspection force in Prussia in 1895 was almost as large as the entire regular army of the United States of that year (27,089). Such a system gave a false sense of security, and pork was still consumed raw with dire results.

There is no doubt that rats harbor the trichinella. They have long been incriminated as the chief source of hog infection; but Spink and Augustine[8] are of the opinion that trichinosis in hogs is usually the result of their ingesting trichinous pork either in garbage or in the offal at times of slaughter. They believe that the infection in rats has its origin in trichinous pork scraps, and that it may be transmitted from rat to rat through cannibalistic habits, but that its return to swine through rats seldom occurs.

INCIDENCE: REPORTS IN THE LITERATURE

Hundreds of cases of trichinosis[9,10] have been recorded in American literature since Bowditch described his findings in 1842. While it is not considered to be so common as many infectious diseases, it does occur far more frequently than the published case reports and vital statistics indicate. Recent statistical studies, based on actually finding the parasites, show that trichinosis is a common disease in this country, and that the majority of cases are of such a mild form that they often pass unrecognized. In 1931 Queen,[11] by artificial digestion of fifty grams of diaphragm from 344 consecutive autopsies in Rochester, New York, found 17.5 per cent contained Trichinella spiralis. None of these cases gave a history of trichinosis, although some gave a vague "rheumatic" history. In a second series of fifty-eight cases in Boston, Queen found 27.6 per cent positive. Riley and Scheifley,[12] in a study of the diaphragms of 117 cadavers in Minneapolis in 1934, found 17.1 per cent positive for trichinella by pressing the muscle between glass slides. Hinman,[13] in 1936, examined ten grams of diaphragm, by the digestion method, from two hundred autopsies in New Orleans, and found only 3.5 per cent positive. Undoubtedly, he would have found a higher percentage had he used the fifty-gram quantities digested by Queen. Hall and Collins[14] reported 13.67 per cent of three hundred human diaphragms in Washington, D. C., positive for trichinella, using combined digestion and microscopic methods.

INCIDENCE IN SAN FRANCISCO

Recently we[15] reported that 24 per cent of the diaphragms from two hundred autopsies in San Francisco were positive for trichinella, using fifty-gram quantities by the digestion method. The diaphragms from an additional twenty-five new-born infants gave negative results. Living larvae were found in all the positive cases in San Francisco, but the number was usually small, being less than twenty to each fifty grams of muscle in 79 per cent of the cases. None of the clinical records of the positive cases revealed a definite history of trichinosis. Many of the case histories recorded "rheumatic" or "muscular" or joint "pains," "gastro-intestinal upsets" and the like, but these were as plentiful in the negative as in the positive cases. The results of these studies in six large, widely separated cities indicate that the actual incidence of trichinosis in the United States is rather high—averaging 15.6 per cent, or one in every six individuals.

Vital statistics of the Department of Health of San Francisco for the years 1931 to 1935 show a reported incidence of trichinosis, ranging from 0.0016 to 0.0044 per cent of the total population for each year. Those for the State of California, for the years 1932 to 1936, range from 0.0014 to 0.0006 per cent. A study of the sources of infection in 311 cases of trichinosis in California shows that 50 per cent were caused by the eating of salami or mettwurst sausages. The striking discrepancy between the number of cases of trichinosis reported, and the number of positive cases found at autopsy, demonstrates that the milder forms and sporadic cases of the disease usually pass unrecognized.

LIFE CYCLE OF TRICHINELLA SPIRALIS

Knowledge of the life history of the trichinella and the pathology of the disease is essential to an understanding of the symptomatology of trichinosis. Man is an accidental host to the parasite when he ingests infected meat. Pork is the usual offender; but a small epidemic due to bear meat[16] has been reported in this State.

Digestive juices liberate the encysted larvae, which pass into the upper intestine. In the course of two or three days they mature, copulate and, as early as the fourth day, the females, having burrowed into the mucosa, start bearing their young into the lymph spaces. During several weeks the

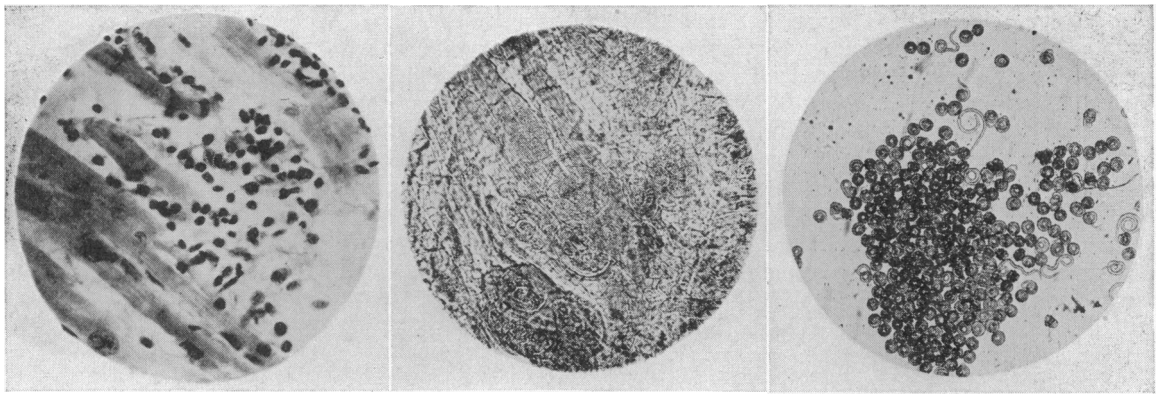

Fig. 1 Fig. 2 Fig. 3

Fig. 1.—Photomicrograph of cardiac muscle, showing necrotic muscle-fibers infiltrated by leucocytes, but no trichinella larvae. (X450).

Fig. 2.—Photomicrograph of sausage pressed then between glass slides, showing many encysted trichinella. (X40).

Fig. 3.—Photomicrograph of living trichinella larvae in the sediment of a digested human diaphragm. (X25).

female ejects a total of 1,000 to 1,500 actively motile young, which migrate and are carried by the lymphatics into the general circulation. The entire body is flooded with enormous numbers of embryos, which increase rapidly in size to almost ten times their original length. Many penetrate the skeletal muscles, become surrounded by a capsule of connective tissue and, in the course of time, often calcify, but may remain alive for many years. Larvae have been found in almost every tissue, fluid, and excretion of the body, but those which do not enter voluntary muscles usually die rapidly.

FACTORS CONCERNED IN THE LOCALIZATION OF TRICHINELLA LARVAE

It has long been known that the circulating trichinella invade such muscles as those of the diaphragm, tongue, larynx, and eye, the masseter and intercostal muscles, more than others. This has been explained by the fact that these are more active than other muscles. However, Berger and Stähelin [17] could demonstrate no quantitative relationship between the activity of a muscle and the number of trichinella it contained, using one paralyzed and one normal leg of animals infected experimentally.

Scheifley [18] investigated the rôle of increased blood flow in localization of the larvae by the removal of the lumbar sympathetic chain and ganglions from one side of dogs. Subsequent infection with trichinella revealed no significant change in localization of the larvae between the normal limbs and those with increased blood flow.

Lewis [19] found that the muscles favored by trichinella contained far less glycogen than those which are relatively spared. The diaphragm of normal guinea pigs contains only 7.2 milligrams per cent of glycogen, the masseter muscles 16.1, while those of the forelegs contain 488.1. He depleted the glycogen content of some of the animals by insulin, and administered large quantities of dextrose to others and infected all with trichinella. Dextrose lessened the migration of the parasites into the muscle, while insulin favored it. This is an encouraging step toward clarifying the question of specificity of localization of trichinella.

PATHOLOGIC CHANGES

The changes in the muscle during trichinous invasion are summarized from Sobel.[20] About the eighth to tenth day of the infection, embryos are found in the skeletal muscles, their long axis parallel to that of the muscle fiber. The fibers lose their striations and assume a finely granular appearance. With eosin-hematoxylin stain, the granules are a blue-violet color instead of the pink of normal muscle. This basophilic degeneration starts near the parasite and extends along most of the length of the muscle fiber. The trichinella curls up within the fiber, and the latter swells to two or three times its normal thickness. The muscle nuclei, normally close to the sarcolemma, increase in number and size, and move centrally about the parasite, become pale-staining and eventually degenerate. The granular degenerated muscle fiber assumes a more homogeneous compact appearance, forming a well-circumscribed elliptical mantle about the coiled worm. An interstitial myositis accompanies these changes from the beginning with infiltration of polymorphonuclears, eosinophils, and lymphocytes. The mesenchymal granulation tissue encircles the parasite with connective tissue, which later becomes hyalinized collagen of considerable thickness. Calcification may begin as early as the fifth month.

Trichinous myocarditis is not a specific picture. There is an active focal cellular infiltration of the myocardium, with lymphocytes, eosinophils, and polymorphonuclears, with necrosis and fragmentation of the muscle fibers apparently caused by the migrating larvae. Figure 1 is a photomicrograph of the cardiac muscle of a woman of sixty-four, who succumbed to trichinosis during the third week of her illness. The eosinophil count reached 39.5 per cent during the second week. Encysted larvae are rarely, if ever, found in the heart muscle. We have examined microscopically the hearts of two patients dead of trichinosis, and hearts of many rats with skeletal muscles peppered with encysted larvae, but have never encountered one encysted in the heart. The hearts of fifteen humans with encysted trichinella in their diaphragms at autopsy

failed to yield a single larvae by the digestion-concentration method.[15]

The meninges of patients exhibiting neurological manifestations may show marked infiltration with lymphocytes, plasma cells, fibroblasts, macrophages, and masses of eosinophils surrounding embryonic trichinella.[21] The brain itself may show granulomatous nodules, with or without parasites, and perivascular infiltrations of polymorphonuclears, lymphocytes, plasma cells, gitter cells, and fibroblasts.[22]

SYMPTOMATOLOGY

The symptomatology of the usual form of trichinosis may be closely correlated with the life history of the parasite. The maturation of the worms in the intestines corresponds to the gastro-intestinal upsets, nausea, vomiting, diarrhea, colic, and fever in the early stage of trichinosis. The period of dissemination of the embryos is marked by muscle aches, difficult and painful mastication, speech and respiration, petechial hemorrhages, edema, and eosinophilia. Spink and Augustine,[9] in an analysis of thirty-five cases of trichinosis, call attention to the fact that many do not exhibit a sufficient number of these symptoms to be readily diagnosed.

Trichinosis is comparable with any generalized bacterial infection. The chief difference is that the embryos of the trichinella are much larger than bacteria. The lesions produced are essentially a combination of toxic manifestations and embolic phenomena.

Myocarditis is one of the most serious, and not so uncommon complications of trichinosis.[23] It is frequent in severe infections, and is seen usually in patients dying in the fourth to eighth week of the disease. Cheney [24] has called attention to the occurrence of extreme hypotension in trichinosis.

It is not unusual to observe neurological manifestations in trichinosis, since the embryos invade the spinal fluid and brain. Most and Abeles [22] recently reviewed this subject, listing cases simulating meningitis, acute and chronic encephalitis, ocular disturbances, diplegia, deafness, and the syndrome of amyotrophic lateral sclerosis.

DIAGNOSIS

The diagnosis of a case of trichinosis should not be difficult, if it follows the common clinical course. A febrile disease with gastro-intestinal symptoms, muscle aches, and edema of the eyelids, calls for a blood count. Most cases of trichinosis will show a moderate leukocytosis, with an eosinophilia. The eosinophils usually increase rapidly, reaching a peak in the third or fourth week. We have also observed this repeatedly in experimental trichinosis in animals. The eosinophils in human trichinosis may mount to 75 to 90 per cent, although counts of 30 to 40 per cent are more frequently encountered.

The finding of the larvae in the body or body fluids of the patient makes the diagnosis certain. Examination of the stool for the parasites is often advised, but this procedure is rarely rewarded with success. Eosinophils have been found in the stools of trichinosis patients.[25] The laking of large quantities of blood or searching the sediment of spinal fluid is rarely satisfactory. Muscle biopsies, when obtainable, may prove satisfactory if the infestation is heavy, but there may be no parasites found in the excised tissue. Biopsy material or suspected meat is usually examined by one of three methods: (1) Portions of the material are pressed thin between glass slides and examined microscopically for encysted parasites. This is simple and rapid, and yields highly satisfactory results when the muscle is heavily infected. Figure 2 is a photomicrograph of a bit of sausage handled in this manner. This meat was responsible for an outbreak of trichinosis in Lower Lake, California. (2) Stained sections are essential for observing histologic changes in trichinous tissue; but unless the parasites are present in large numbers they may be missed if only a few slides are prepared. (3) The most satisfactory method in our hands for studying suspected material is by digesting the muscle with liberation and concentration of the larvae.[15] Figure 3 is a photomicrograph of the concentrated sediment from a human diaphragm.

SKIN AND SEROLOGIC TESTS

Within the last decade skin and serologic tests have been found of value in doubtful cases of trichinosis. Bachman [26] was the first to use trichinella antigen for diagnostic purposes. Augustine and Theiler [27] applied the test to human beings, and concluded that the skin test and precipitin reaction are of specific value in the diagnosis of trichinosis. Many other investigators have confirmed their findings. Recently, Spink [28] reported fifty-nine positive skin tests in sixty patients with trichinosis. The single negative reaction was elicited in a moribund patient, whose muscles at autopsy were shown to be heavily infiltrated with trichinella.

McCoy, Miller, and Friedlander [29] found that 92 per cent of thirty-six persons ill with trichinosis gave positive skin reactions, and Kaljus [30] reports 74 per cent of sixty-six cases were positive.

Skin Reactions.—Spink [28] describes two types of skin reactions to the antigen, an immediate and a delayed. The immediate type usually is not obtained until the second week of the infection. Within five to ten minutes after intradermal injection of the antigen a blanched wheal appears, sometimes with pseudopodia, but always with a surrounding zone of erythema. The reaction usually reaches its maximum within an hour, when it gradually subsides. The delayed type of skin reaction consists of an erythematous flare, following injection, which quickly subsides. Then, in twelve to twenty-four hours there is a red, slightly edematous, tender area from 1 to 3 centimeters in diameter, at the site of injection. This type, he believes, occurs early in the course of the disease, and later changes to the immediate type.

The precipitin test is performed by carefully layering 0.3 or 0.5 milliliter of a 1-100 dilution of trichinella antigen over a similar amount of serum in a small serological tube. The control consists of layering saline diluting fluid over the serum. Both tubes are incubated for an hour in a 37.5 degrees centigrade water bath. An opaque whitish ring at the junction of the antigen and serum indicates a positive test. Spink states that the precipitin test

usually becomes positive by the end of the fourth week.

We have recently investigated the skin reactions to trichinella antigen. The antigen is prepared in general according to the methods of Bachman, and others.[28,29] Adult white rats of the Wistar strain are fed about twenty free trichinella larvae per gram, by means of a stomach tube. Our strain of Trichinella spiralis was isolated from a human diaphragm, and is kept alive in the rat colony. After about five weeks the infected animals are sacrificed, skinned, eviscerated, and ground in a meat chopper. The meat is thoroughly digested in six to twelve hours by agitation in an aqueous solution of one per cent granular pepsin and 0.7 per cent hydrochloric acid in a 37.5 degree centigrade incubator. The lying larvae are thus freed from the meat and their capsules. The digest is passed through a twenty-mesh, then a sixty-mesh sieve, to remove undigested particles and bone, and placed in a large glass separatory funnel. The larvae settle to the bottom, are drawn off into a beaker and washed with tap water until the washings are clear and no débris is seen microscopically. The concentrate of larvae is dried rapidly in open Petri dishes within a vacuum desiccator in the incubator. It is important that this process be rapid to prevent bacterial growth, which would complicate the antigenic specificity. The larvae are then extracted with ether for twenty-four hours and again dried. This powder is the antigen. A 1-100 dilution of the powder is prepared in a small flask, using a buffered saline solution (0.5 per cent NaCl, 0.143 per cent Na_2HPO_4, 0.036 per cent KH_2PO_4 and 0.4 per cent phenol for preservative) with a p_H of 7.1 This is permitted to extract for twenty-four hours at room temperature, then ground in a ball mill for another twenty-four hours. The resultant mixture is passed through a Seitz filter. The clear fluid, considered to be a 1-100 dilution of the antigen, is further diluted with the saline solution to make 1-500 and 1-10,000 dilutions of the original antigen, and placed in sterile vials with rubber stoppers of the type readily punctured by an hypodermic needle. Vials of the saline diluting fluid are prepared as controls.

The tests are made by the intradermal injection of 0.1 cubic centimeter of diluted antigen into the skin of one forearm with a similar injection of control solution into the other arm. The tuberculin type of syringes with short bevel, 26-gauge, hypodermic needles are best suited to these procedures. We have followed the methods of McCoy, Miller, and Friedlander, of routinely using the 1:10,000 dilution of the antigen for the first injection. If this is negative, a second test is made in about twenty-five minutes, using the 1:500 dilution. The immediate type of reaction is not considered positive unless the wheal is at least 7 millimeters in diameter and the zone of erythema 20 millimeters.

To date we have tested only five cases of clinically active trichinosis, ranging from the third to the sixth week of illness. These have all shown positive skin tests of the immediate type. One case of illness with a history, signs and symptoms of trichinosis and 16 per cent eosinophilia, on the tenth day gave a delayed type of reaction with a 25 millimeter tender area of erythema and edema. When tested on the thirtieth day, at which time the eosinophils had mounted to 54 per cent, the reaction was of the immediate type with a 10-millimeter wheal and 30-millimeter zone of erythema. A precipitin test on the serum from this patient on the thirtieth day of illness, using a 1-100 dilution of trichinella antigen, was also positive.

COMMENT

In view of our finding at autopsy that 24 per cent of the diaphragms in San Francisco contained trichinella with no history of trichinosis,[15] we are curious as to the number of persons living in this area with no history or symptoms of infection who show a sensitivity to the trichinella antigen. We have tested only sixty-three such individuals thus far, but have found 12.7 per cent of them give the immediate type of reaction and 11.9 per cent the delayed type. If all of the delayed types are specific reactions—and we are not convinced that they are—the total per cent of positive skin tests in this series is 24.6. This is unbelievably similar to the 24 per cent found at autopsy.

McCoy, Miller, and Friedlander found 18 per cent of 104 control individuals in Rochester, New York, and 6.5 per cent of forty-seven controls in San Francisco gave positive immediate reactions to the trichinella antigen. They state that delayed reactions were sometimes noted after twenty-four hours, "but their presence could not be correlated with the immediate reaction, and they have been disregarded."

Theiler, Augustine, and Spink[31] note that patients may show a positive skin reaction as long as seven years after infection with Trichinella spiralis. Thus, it is not possible by means of the skin test alone to distinguish between acute trichinous infections and those which occurred some years previously. We conclude from our few data that even the subclinical cases of trichinosis, which must greatly exceed the clinical ones, show sensitivity to the antigen.

TREATMENT

Patients with trichinosis should be treated as those with any other general febrile disease, by bed rest, adequate fluids, nourishment, and relief of pain. A preliminary purge has been recommended to remove such parasites as may still be free in the intestines. This may be of questionable value, since the females are usually buried in the mucosa.

A variety of agents have been employed in attempts to destroy the parasites in the body. Neoarsphenamin, antimony and potassium tartrate, acriflavin, rivanol, gentian violet, metaphen, Lugol's solution and sodium iodid were all found ineffective in experimental trichinosis by Miller, McCoy, and Bradford.[32] Miller, in a personal communication, states that further work indicates that there may be some value to the use of thymol, but that toluol and xylol are ineffective.

Since there are reports that the liberal use of alcoholic beverages, while ingesting trichinous

meat, offers protection, we are now investigating this subject. Our results thus far indicate that such is really the case, but that the mechanism is one of interference with digestion and failure to liberate the larvae rather than a toxic action on the worm.

Blumer [33] questions the desirability of destroying, at one time, the enormous numbers of trichinella which are present in the body. It is possible, if an effective parasiticide were discovered, that the destruction en masse might result in a sudden flooding of the system with large quantities of toxic substances. Obviously, the larvae cannot be removed from the patient after they have left the intestinal tract and become encysted in the muscles. The administration of vitamin D [34] and calcium [35] has been advised to accelerate calcification of the capsule.

McCoy [36] has shown that immunity can be developed in rats, and others [37,38] report that while immune serum does not damage the parasites, it apparently neutralizes the toxemia. Salzer [39] was encouraged by his use of serum from recovered patients in treating clinical trichinosis.

COMMENT

It is readily seen that trichinosis is quite a common disease, but that the majority of cases are probably subclinical in type and are not diagnosed. The quantity of parasites ingested by the individual is probably the greatest factor in determining the clinical course. Its recognition depends on a critical history of the patient's illness as to possible sources of infection, examination of suspected meats, and a study of others partaking of the same foods. Patients with gastro-intestinal complaints, fever, vague muscle aches which persist, and an eosinophilia, should have a skin and precipitin test for trichinosis. Biopsy is of value if the parasites are present in sufficient numbers in the excised muscle, but it is an inconvenience to the patient, and frequently cannot be obtained. Skin and precipitin tests have been shown to be of high diagnostic value and may be performed at practically no inconvenience to the patient.

Since a certain number of individuals with no history of infestation show a positive skin test, it must be borne in mind that all evidence must be considered before making a diagnosis of trichinosis, especially in the sporadic cases, and that too much weight must not be attached to any one feature. The history, symptoms, signs, eosinophilia, skin and precipitin tests, must all be properly evaluated.

It is impossible to detect infected pork by practical methods of meat inspection. Therefore, it is necessary for the consumer to assume the responsibility of preventing trichinosis by either avoiding or thoroughly cooking all fresh pork.

SUMMARY

1. Trichinosis is a common disease, but the majority of cases are subclinical in type and are not diagnosed.

2. The incidence of trichinosis, as revealed by actually finding the parasites in autopsy material in six widely separated cities in the United States, averages 15.6 per cent.

3. Pathologic changes in skeletal muscle, heart muscle, meninges, and brain are briefly described.

4. Methods of diagnosis are reviewed. Eosinophilia is the simplest and one of the most reliable diagnostic clinical aids.

5. The technique for skin and precipitin tests, method of preparing trichinella antigen, and results of the tests are outlined.

6. The consumer must assume the responsibility of preventing trichinosis by thoroughly cooking all fresh pork.

Stanford University School of Medicine.

REFERENCES

1. Leviticus 11:7-8, and Deuteronomy 14:8.
2. Brim, Charles J.: Trichinosis—Flesh of the Hog, M. Life, 43:515-530 (Nov.), 1936.
3. Editorial: The Discovery of Trichina Spiralis, Brit. M. J., 2:610 (Oct.), 1930.
4. Bowditch, Henry I.: Trichina Spiralis, Boston M. and S. J., 26:117 (March), 1842.
5. Leidy, Joseph: Proc. Philadelphia Acad. Sc., 3:107, 1847.
6. Zenker, F. A.: Ueber die Trichinen, Virchow's Arch. f. path. Anat., 18:561, 1860.
7. Stiles, C. W.: Trichinosis in Germany, U. S. Dept. Agric. Bureau of Animal Industry Bull., No. 30, 1901.
8. Spink, W. W., and Augustine, D. L.: Trichinosis in Boston, New England J. Med., 213:527-531 (Sept. 12), 1935.
9. Spink, W. W., and Augustine, D. L.: The Diagnosis of Trichinosis, J. A. M. A., 104:1801-1805 (May 18), 1935.
10. Drake, E. H., Hawkes, R. S., and Warren, M.: An Epidemic of Trichinosis in Maine, J. A. M. A., 105:1340-1343 (Oct. 26), 1935.
11. Queen, F. B.: The Prevalence of Human Infection with Trichinella Spiralis, J. Parasitol., 18:128 (Dec.), 1931.
12. Riley, W. A., and Scheifley, C. H.: Trichinosis of Man a Common Infection, J. A. M. A., 102:1217 (April 14), 1934.
13. Hinman, E. H.: Trichiniasis in Louisiana, New Orleans M. and S. J., 88:445-448 (Jan.), 1936.
14. Hall, M. C., and Collins, B. J.: Studies on Trichinosis I, Pub. Health Rep., 52:468-490 (April 16), 1937.
15. McNaught, J. B., and Anderson, E. V.: The Incidence of Trichinosis in San Francisco, J. A. M. A., 107: 1446-1448 (Oct. 31), 1936.
16. Walker, A. T.: Trichinosis—Report of an Outbreak Caused by Eating Trichinous Bear Meat in the Form of "Jerky," J. A. M. A., 98:2051 (July 11), 1932.
17. Berger, E., and Stähelin, A.: Studien über den Mechanismus der Trichinelleninfektion, Centralbl. f. Bakt. Abt., 1, 108:397-401, 1928.
18. Scheifley, C. H.: The Localization of Trichinella Spiralis in the Muscle of Its Host, Am. J. Hyg., 25:349-353 (March), 1937.
19. Lewis, J. H.: Studien über Mechanismus der Trichinelleninfektion, Centralbl. f. Bakt. Abt. 1, 107:107-114, 1928.
20. Sobel, I. P.: Sporadic Trichinosis in Children, Am. J. Dis. Child., 51:367-388 (Feb.), 1936.
21. Hassin, G. B., and Diamond, I. B.: Trichinosis Encephalitis, Arch. Neurol. and Psychiat., 15:34 (Jan.), 1926.
22. Most, H., and Abeles, M. M.: Trichiniasis Involving the Nervous System, Arch. of Neurol. and Psychiat., 37:589-616 (March), 1937.
23. Spink, W. W.: Cardiovascular Complications of Trichinosis, Arch. Int. Med., 56:238-249 (Aug.), 1935.
24. Cheney, G.: Sporadic Trichinosis with Extreme Hypotension, J. A. M. A., 86:1004 (April 3), 1926.
25. Baumgartner, E. A., and Cowles, A.: Trichinosis, with a Report of Two Cases with Eosinophils in the Stools, J. Lab. and Clin. Med., 22:484-489 (Feb.), 1937.
26. Bachman, G. W.: (*a*) A Precipitin Test in Experimental Trichiniasis, J. Prev. Med., 2:35 (Jan.), 1928. (*b*) An Intradermal Reaction in Experimental Trichiniasis, *ibid.*, 2:513 (Nov.), 1928.

27. Augustine, D. L., and Theiler, H.: Precipitin and Skin Tests as Aids in Diagnosing Trichinosis, Parasitology, 24:60 (March), 1932.

28. Spink, W. W.: Trichinella Antigen, New England J. Med., 216:5-8 (Jan. 7), 1937.

29. McCoy, O. R., Miller, J. J., and Friedlander, R. D.: The Use of an Intradermal Test in the Diagnosis of Trichiniasis, J. Immunol., 24:1-23 (Jan.), 1933.

30. Kaljus, W. A.: On the Practical Value of Intradermal Reaction with Trichinelliasis Antigen for Diagnosis of Trichinelliasis in Man. Puerto Rico J. Pub. Health and Trop. Med., 11:768-790 (June), 1936.

31. Theiler, H., Augustine, D. L., and Spink, W. W.: On the Persistence of Eosinophilia, and on Immune Reactions in Human Trichinosis Several Years After Recovery, Parasitology, 27:345-354 (Aug.), 1935.

32. Miller, J. J., McCoy, O. R., and Bradford, W. L.: Intravenous Treatment in Experimental Trichiniasis, J. A. M. A., 98:1242-1245 (April 9), 1932.

33. Blumer, George: Trichinosis, New Eng. J. Med., 214:1229-1235 (June 18), 1936.

34. Barker, F. D., and Wantland, W. W.: Vitamin D and Trichinosis Patients, Science (Supplement), 83:12 (May 1), 1936.

35. Goldschlager, A. I.: Trichinosis, Ann. Int. Med., 8:939 (Feb.), 1935.

36. McCoy, O. R.: Artificial Immunization of Rats Against Trichinella Spiralis, Am. J. Hyg., 21:200 (Jan.), 1935.

37. Schwartz, B.: Trichinosis, J. A. M. A., 69:884 (Sept.), 1917.

38. Hall, M. C., and Wigdor, M.: An Experimental Study of Serum Therapy in Trichinosis, Arch. Int. Med., 22:601 (Nov.), 1918.

39. Salzar, B. F.: Trichinosis, J. A. M. A., 67:579 (Aug. 19), 1916.

DISCUSSION

JOHN J. MILLER, M.D. (Stanford University Hospital, San Francisco).—Splinter hemorrhages under the nails, chemosis of the conjunctiva, and double vision are occasionally observed.

I cannot quite agree with Doctor McNaught's statement that direct examination of the blood and spinal fluid for parasites is rarely satisfactory. On two occasions I have found larvae in the blood. About 40 cubic centimeters of blood are taken, laked with two volumes of distilled water, and then centrifuged down. If any larvae are present, they are readily apparent in the sediment. This method is the quickest and simplest one for confirming the diagnosis. To my mind the procedure next in order is a lumbar puncture. I have seen larvae in the spinal fluid of five patients. Three or four minutes of centrifugation are sufficient. Obviously, the more spinal fluid obtained, the better the chance of finding larvae.

The skin test seems to be of definite value and should be used if antigen is available. While, as Doctor McNaught said, it is not possible by means of the skin test alone to distinguish between active and healed trichinosis, the skin hypersensitivity has a very definite tendency to decrease with time. Therefore, a positive reaction to a high dilution of antigen, 1:10,000 or higher, suggests active infection. We have seen skin reactions in acute trichinosis to a 1:1,000,000 dilution. The use of these dilutions is also important, when it is recalled that the skin test is not strictly specific. When McCoy tested ninety-two persons in southern Louisiana infected with Trichuris trichiura, he found 18 per cent positive to a 1:10,000 dilution, and 62 per cent positive to a 1:500 dilution. This group reaction is, of course, due to the close biological relationship between Trichinella spiralis and Trichuris trichiura.

Eosinophilia is also of the greatest aid in diagnosis. It should be remembered, however, that an absence of eosinophilia in a very sick patient does not rule out trichinosis. In two instances we have noted a drop in eosinophilia to less than 4 per cent within three days of death. Coincidentally, the skin reaction, which had been positive to a high dilution, became very weak shortly before exitus.

With the use of the above procedures a diagnosis can almost always be confirmed. I do not believe that a biopsy is often warranted. If a biopsy is finally done, however, the material should be digested as Doctor McNaught describes, rather than sectioned.

R. D. FRIEDLANDER, M.D. (384 Post Street, San Francisco).—I am glad, for two reasons, to be allowed the privilege of discussing Doctor McNaught's paper: First, because of my interest in trichiniasis, which has led me to follow carefully the literature on the subject for the past five years, so that I feel competent to state that Doctor McNaught's paper is not only the most comprehensive review of the subject to date, but it adds original findings that enhance to a considerable degree our present knowledge of trichiniasis. The second reason is that I should like to amplify several points that have been touched upon by Doctor McNaught.

Those acquainted with this problem know that my interest has been centered mainly in the intradermal test as a specific diagnostic measure. It was the original hope that the test, if positive, would give unequivocal evidence of an acute infestation by the larvae of Trichinella spiralis. We know now that, while there is no doubt about the specificity of the test, there may be some doubt about the acuteness of the infection when the test is positive, because it has been shown that individuals may exhibit a positive intradermal reaction as long as seven years after the first infection. Recent work by Spink, however, may help somewhat to clear up this problem. Spink has reported two types of intradermal reactions to trichinella antigen: an immediate, and a delayed. The immediate reaction usually does not occur until some time around the second week of illness, whereas the delayed reaction is said to occur earlier in the course of the disease. There has always been some doubt about the specificity of the delayed reaction; but if Spink's findings are corroborated by further work the intradermal test might serve not only as a diagnostic aid, but also as an indication of the stage of infection in new cases. What one might expect of the intradermal test, applied to an individual suffering from trichiniasis a second time, has not yet been determined. It is apparent that the allergic aspect of this problem must be of considerable importance. For the present, however, we must still rely upon a proper evaluation of "the history, symptoms, signs, eosinophilia, intradermal and precipitin tests" for the diagnosis of trichiniasis.

The diagnosis having been made, one is next interested in therapy. There is no specific remedy for trichiniasis as yet, so that prevention would seem to be of major importance, if members of the medical profession feel that this disease is on the increase. Doctor McNaught and, among others, Doctor Blumer of Yale Medical School, feel that the consumer must assume the responsibility of preventing trichiniasis by either avoiding or thoroughly cooking all pork. Doctor Blumer felt that the individuals responsible for the occurrence of the disease were not the meat dealers, but the consumers.

I cannot help but feel that this is a highly disputable opinion, particularly on the part of the profession. It seems all the more inconsistent, if one considers the fact that prevention of such diseases, which may be transmitted to the consumer in food products or by food handlers, has never been accomplished satisfactorily by the assumption of responsibility by the consumer. It is comparable to the statement that if the public consumes milk from tuberculous cows, it deserves to contract tuberculosis; or if the public consumes milk or water from typhoid-contaminated sources, it is responsible for the occurrence of typhoid fever. While these statements may be literally true, such has not been the stand of local or state health departments. The only justification for such a stand regarding trichiniasis is that, because it is not contagious, it could never assume large epidemic proportions; hence the attitude of *caveat emptor*.

This brings up the point that an important piece of work of considerable bearing on the epidemiologic aspect of this disease has been either overlooked or ignored. In 1932, Augustine and Theiler reported the results of precipitin and intradermal tests on a small number of swine infested with Trichinella spiralis. These tests were found to be positive in pigs, which, after slaughter, showed no larvae on extensive microscopic examination of muscle slips from the tongue, diaphragm, intercostal and masseter muscles. Yet after artificial digestion of the same muscular tissue, in the same manner as described by Doctor McNaught, large numbers of living trichinella larvae were obtained. The conclusion was that the precipitin and intradermal tests were more accurate than muscle examination. So far as I know, intradermal tests on swine have never been done

on a large scale to confirm this work. Nevertheless, if the findings of these workers should be definitely confirmed, then intradermal tests in trichinous pigs would be just as specific as tuberculin tests in tuberculous cows. The opinion that has been held in the past, that we must have trichiniasis because of the inability to detect infested swine, would then be tenable no longer.

E. M. Butt, M.D. (University of Southern California School of Medicine, Los Angeles).—Our attention has been drawn to the subject of trichinosis by the startling figures obtained by a few recent workers in determining the prevalence of trichina infestation in cadavers. These figures are from widely separated localities and, excepting the report from New Orleans, indicate an incidence of trichina infestation in well over 15 per cent of the cadavers examined. Yet, as McNaught has pointed out, the vital statistics of the State of California show a very low incidence of the disease. This discrepancy has been dismissed quickly with the conclusion that, clinically, the disease is rare, and that subclinical infestation is common. However, quantitative evaluation of infestations would indicate that such an inference is not true in a certain percentage of positive cases. It follows, therefore, that patients with trichinosis are not seen medically or that our training and diagnostic methods are faulty and require scrutiny. Aside from the clinical importance of trichinosis, there is a public health aspect of utmost interest.

Recently, we have completed the examination of 150 diaphragms by the digestion method. These specimens have been taken at random from our autopsy service. The total percentage of positive findings was 17.3 per cent. Further analysis of these figures revealed a higher percentage of infestation in females than in males. This is due to the high incidence of trichina in diaphragms of colored females, a figure which in our small series was close to 50 per cent. Thirty-seven per cent of the diaphragms from Mexicans and Negroes, both males and females, were positive for trichinae.

It is still too early to adequately evaluate the diagnostic importance of the skin test. The few clinical cases that we have seen have all given an immediate positive reaction to the antigen. However, there are reports in the literature that indicate that such is not always the case. Furthermore, positive skin tests have been obtained in individuals with Trichuris trichiura infestation. So far, little attention has centered around the trichina skin test in hyperergic patients. These and other aspects must be taken into account before the skin test can be considered reliable in the diagnosis of trichinosis.

Trichinosis is a subject of considerable clinical and public health importance. Doctor McNaught's admirable paper should help to create more interest in the subject.

SNAKE VENOM: ITS USE IN POSTOPERATIVE HEMORRHAGE OF THE EYE*

By W. F. Swett, M.D.
San Francisco

Discussion *by Warren D. Horner, M. D., San Francisco; Frederick C. Cordes, M. D., San Francisco.*

THE management of postoperative hemorrhage, following major procedures on the eye, is always difficult to control, and the usual procedures are notoriously ineffective. These cases have always been a source of worry, and in my effort to find something to control this situation I was encouraged by reports of Peck [1] (1931), McFarlande and Barnett [2] (1934), and Dack [3] (1935), in their use of moccasin venom in the treatment of hemorrhagic disease.

During the past year I have had several stubborn postoperative hemorrhage cases which were responsible in my using the snake venom therapy, in an effort to find a good postoperative treatment in this distressing complication.

MOCCASIN VENOM

The moccasin venom was prepared in a concentration of 1/3000, in a physiological saline solution with 1/10,000 merthiolate being added as a preservative. According to these authors, it was efficacious in functional uterine bleeding, epistaxis, and hematuria in the Henoch-Schönlein syndrome, in thrombocytopenic purpura, in multiple heredity telangiectasis, and in hemoptysis from bronchiectatic cavities. The more recent applications have shown that the venom is excellent as a coagulent in local intractible bleeding, and was found especially effective in cases of functional uterine bleeding and idiopathic nasal hemorrhages. This led to its being used preoperatively, in patients predisposed to excessive hemorrhage, with equally good results. Hemophitic blood, which normally clotted in twenty to forty-five minutes, was clotted in seventeen seconds by a 1/10,000 dilution of venom, and has been used successfully in managing hemophiliac hemorrhages following dental extraction, tonsillectomy, epistaxis, and oozing from abdominal wounds.

In giving the venom, ecchymosis may develop at the site of injection in the first twenty-four hours, and most patients develop a reaction of hypersensitivity in approximately ten to fourteen days; however, the reaction is always local, and characterized by a hot, tender swelling at the point of injection only. No general reaction may be feared. In the six cases that I have used it on up to date, I have had no reaction whatever, either local or general.

The continuous oozing of blood from the iris or the wound into the anterior chamber, following cataract extractions, prolongs the healing and in many instances results in the failure of the wound to close, or even a painful eye with rupture of the wound and prolonged seepage from the anterior chamber.

In the first case, hemorrhage occurred the first day following operation and continued to ooze in spite of all treatment for ten days. I decided to use the moccasin venom put out by Lederle, and was very pleasantly surprised when the oozing stopped immediately after the first injection of .4 cubic centimeter. As soon as the hemorrhage was checked, the blood disappeared rapidly from the anterior chamber and the wound was closed completely four days later. I have used it in four cases since with identical results. These results have been so satisfying that I have come to look upon the venom as indispensable in the control of postoperative hemorrhage. To date I have only administered it in those cases which showed a tendency to hemorrhage after operation, and found that .5 cubic centimeter given daily for one week has been sufficient. I feel that the ideal method of use would be to give these injections previous to operation to prevent the complications rather than to correct them. I have not gone into this phase of the subject because I first wanted to demonstrate to my satisfaction the action of the venom on actively hemorrhaging cases.

* Read before the Eye, Ear, Nose, and Throat Section of the California Medical Association at the sixty-sixth annual session, May 2–6, 1937.